UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date 23-October-2014

Subject: **Mesotrione** in/on Mesotrione-Tolerant Soybean. **Summary of Analytical Chemistry and Residue Data.**

PC Codes: 122990	**DP Barcode:** D414413; D414598
Decision No.: 476009	**Registration No.:** 100-1131 Callisto® Herbicide
Petition No.: 3F8160	**Regulatory Action:** Section 3 Registration
Risk Assessment Type: not applicable	**Case No.:** 7256
TXR No.: not applicable	**CAS No.:** 104206-82-8
MRID Nos.: see table below	**40 CFR:** §180.571

From: Tom Bloem, Chemist
Risk Assessment Branch 1/Health Effects Division (RAB1/HED; 7509P)

Through: George F. Kramer, Ph.D., Senior Chemist
RAB1/HED (7509P)

To: Kathryn Montague/Michael Walsh RM 23
Registration Division (RD; 7505P)

Summary of Submitted/Reviewed Residue Chemistry Studies

OCSPP 860 Series Guideline	MRID Number	Title
860.1300	48996202	Dohn, D (2012). ^{14}C-Mesotrione – Nature of the Residue in Herbicide Tolerant (HT) Soybeans. Report No. 1943W. Unpublished study conducted by Syngenta. 530 p.
860.1500 & 860.1520	48996201	Oakes, T. (2012). Mesotrione SC (A12738A) - Magnitude of the Residues in or on Mesotrione Tolerant Soybeans. Report No.: T000908-07. Unpublished study prepared by Syngenta Crop Protection, LLC. 420 pages.
860.1500	49191501	Oakes, T. (2013). Mesotrione SC (A12738A) - Magnitude of the Residues in or on Mesotrione Tolerant Soybeans (Event SYHT0H2) USA 2012. Report No.: TK0112226. Unpublished study prepared by Syngenta Crop Protection, LLC. 94 pages.

TABLE OF CONTENTS

1.0 Executive Summary

Background: Mesotrione (2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione) is a triketone herbicide which inhibits the enzyme p-hydroxyphenyl-pyruvate dioxygenase (HPPD), disrupting carotenoid biosynthesis. This process leads to the destruction of chlorophyll, resulting in a bleaching effect in susceptible plants. Mesotrione is intended for preemergence and postemergence use for the selective control of annual broadleaf weeds. Mesotrione is currently registered for application to asparagus, berry group 13, field corn, seed corn, yellow popcorn, sweet corn, cranberry, flax, grasses grown for seed, lingonberry, pearl millet, oat, okra, rhubarb, sorghum (sweet and grain), soybean, and sugarcane with tolerances for residues of mesotrione *per se* of 0.01-1.5 ppm.

Syngenta is currently proposing pre-/post-emergent application to mesotrione-tolerant soybean and the establishment of a tolerance for residues of mesotrione *per se* in/on soybean seed of 0.02 ppm. Syngenta also indicated that they intend on bringing the soybean variety SYNHT02R to market and indicated that this variety has been genetically modified to express the avhppd-03 gene derived from oat (*Avena sativa* L.) and the PAT gene from *Streptomyces viridochromogenes* (e-mail from Dr. Jerry Wells of Syngenta to Michael Walsh of RD). The avhppd-03 gene confers tolerance to mesotrione as it encodes a HPPD enzyme with a lower binding affinity to mesotrione than the native HPPD enzyme. The PAT gene encodes the enzyme phosphinothricin acetyltransferase which acetylates the active ingredient glufosinate (glutamine synthetase inhibitor) to the non-herbicidal N-acetyl glufosinate. It is noted that mesotrione is currently registered for preemergent application to mesotrione-tolerant soybean with an established tolerance for residues of mesotrione *per se* in/on soybean seed of 0.01 ppm (grazing/feeding soybean forage/hay is prohibited; D358159, S. Levy, 5-Aug-2009).

Proposed Use: The petitioner provided a proposed Callisto® Herbicide (EPA Reg. No. 100-1131; suspension concentrate (SC); 4 lbs ai/gallon) label which included instructions for pre-emergent application (0.20 lb ai/acre) and post-emergent foliar application up to the R1 crop stage (0.09-0.20 lb ai/acre) to mesotrione-tolerant soybean (0.31 lb ai/acre/year). Provided the label is revised to prohibit the grazing/feeding of soybean forage/hay, HED concludes that the proposed application directions are adequate. A revised Section B is requested.

Nature of the Residue - Primary Crops: Field corn (preemergent and foliar application), peanut (preemergent application), and cranberry (foliar application) metabolism studies conducted with [cyclohexanedione-2-^{14}C]mesotrione and/or [^{14}C-phenyl]mesotrione were previously submitted and reviewed (D245477, S. Levy, 6-Jun-2001; D283827, W. Cutchin, 12-Jan-2005; D326898, S. Levy, 2-Mar-2007). These data indicate that the phenyl and cyclohexanedione rings may be cleaved during metabolism with the phenyl ring forming 2-nitro-4-(methylsulfonyl)benzoic acid (MNBA) and 2-amino-4-(methylsulfonyl)benzoic acid (AMBA) and the cyclohexanedione degraded to a variety of metabolites and/or natural products (mesotrione may also undergo hydroxylation to form 4-OH-mesotrione; see Attachment 3 for structures). Based on these data, HED concluded that the residue of concern in the currently-registered crops for tolerance expression and risk assessment purposes is mesotrione *per se*. It was noted that since the cranberry study was conducted with only [^{14}C-phenyl]mesotrione, the requirements for plant metabolism data in three dissimilar crops had not been fulfilled, and that additional plant metabolism data may be required to support future uses.

In support of the current petition, Syngenta submitted a mesotrione-tolerant soybean (SYHT04R soybean) metabolism study which employed an application scenario similar to the proposed application scenario. Total radioactive residues (TRRs) in the dried seed were low (0.039-0.104 ppm) with mesotrione, 4/5-hydroxy-mesotrione, MNBA, and/or AMBA identified at 3-10% TRR (total identified at 6-16% TRR). The study indicated that mesotrione is metabolized in SYHT04R soybean via hydroxylation of the cyclohexanedione ring followed by cleavage of the phenyl-cyclohexanedione ring bridge to form MNBA and AMBA; mesotrione and/or the identified metabolites may also be metabolized to a variety of minor metabolites and/or incorporated into natural products. Based on these data, HED concludes that the nature of the residues in SYHT04R dried soybean seed following pre-emergent and foliar application is understood with mesotrione *per se* as the residue of concern for tolerance enforcement and risk assessment purposes. Since a grazing/feeding restriction for soybean forage/hay is required, defining the residues of concern in these commodities is unnecessary.

HED notes that the metabolism study was conducted with SYHT04R soybean while SYNHT02R soybean is the variety Syngenta will bring to market. Both of these varieties were genetically modified to express the avhppd-03 gene derived from oat (*Avena sativa* L.). SYNHT02R differs from SYHT04R in that it also contains the PAT gene from *Streptomyces viridochromogenes*; the PAT gene encodes the phosphinothricin acetyltransferase enzyme which acetylates glufosinate ammonium to the non-herbicidal N-acetyl glufosinate (see Attachment 4). The Food and Drug Administration review of glufosinate ammonium tolerant corn indicated that the phosphinothricin acetyltransferase enzyme derived from the *Streptomyces viridochromogenes* PAT gene is specific for glufosinate ammonium while not effecting L-glutamate or other amino acids (http://www.fda.gov/Food/FoodScienceResearch/Biotechnology/Submissions/ucm161145.htm). Based on the structurally similarity of glufosinate ammonium and glutamate and since the phosphinothricin acetyltransferase enzyme did not alter glutamate, HED concludes that it is unlikely that the phosphinothricin acetyltransferase enzyme will alter mesotrione or its metabolites. Therefore, the SYHT04R metabolism data are adequate to represent metabolism of mesotrione in SYNHT02R.

Nature of the Resdiue - Rotational Crops: A confined rotational crop study conducted with cyclohexanedione-2-^{14}C]mesotrione and [^{14}C-phenyl]mesotrione has been previously submitted and reviewed (D274111, S. Levy, 26-Apr-2001; D245477, S. Levy, 6-Jun-2001). Wheat and soybeans were planted 30 days after soil treatment at ~0.275 lb ai/acre (1.4x/0.9x the proposed maximum single/seasonal rate). Endive, radish, and wheat were planted at 120 (both labels) and 300 (phenyl label only) days after soil treatment at 0.412 lb ai/acre (2.1x/1.3x the proposed maximum single/seasonal rate). The study indicated that leafy and root crops could not be planted at the 30 day interval because of phytotoxicity. Based on the identified residues, mesotrione is metabolized in rotational crops via a route similar to that demonstrated in primary crops. HED concluded that for tolerance expression and risk assessment purposes, the residue of concern in/on rotational crop commodities is mesotrione *per se*.

Nature of the Residue - Livestock: Ruminant (dietary burden of ~10 ppm; 7 consecutive days) and poultry (dietary burden of ~10 ppm; 10 consecutive days) metabolism studies conducted with cyclohexanedione-2-^{14}C]mesotrione and [^{14}C-phenyl]mesotrione has been previously submitted and reviewed (D245477, S. Levy, 6-Jun-2001; D283827, W. Cutchin, 12-Jan-2005; D274111, S. Levy, 26-Apr-2001). Based on the results of the dairy cow metabolism studies, it was proposed that mesotrione is metabolized by the reduction of the nitro group to an amino group, leading to the formation of the metabolite AMBA. In addition, separation of the phenyl and cyclohexanedione rings may occur with the cyclohexanedione ring metabolized and incorporated into natural products such as lactose. In the poultry metabolism study, mesotrione was the primary residue found in eggs and edible tissues; however, incorporation into natural components such as palmitic, oleic, and stearic acid was also demonstrated. HED concluded that for tolerance expression and risk assessment purposes the residue of concern in/on livestock commodities is mesotrione *per se*.

Magnitude of the Residue - Proposed Crops: The number and geographical representation of the submitted mesotrione-tolerant soybean field trial data are adequate and resulted in mesotrione residues of ≤0.025 ppm following treatment using the proposed application scenario. In addition, an adequate processing study has been submitted which yielded the following processing factors for mesotrione *per se*: soybean flour (1.75x), hulls (0.50x); aspirated grain fractions (AGF; 0.50x); meal (0.25x); refined oil (0.25x); and crude oil, milk, tofu, soy sauce, and miso (<0.25x).

Magnitude of the Residue - Livestock and Rotational Crops: Based on the results of the livestock metabolism studies and the dietary burdens associated with all registered/proposed uses, residues in livestock are anticipated to be insignificant. In addition, based on the proposed application rate, rotational crop restrictions, and results from the confined/field rotational crop studies, residues in rotational crops are also expected to be insignificant.

2.0 Recommendations

Provided the petitioner submits revised Sections B and F, HED concludes that the residue chemistry database supports the establishment of permanent tolerances listed in Section 2.2.2. A human-health risk assessment is forthcoming.

2.1 Data Deficiencies/Data Needs

No data deficiencies were identified for the current petition. It is noted that future petitions may require additional plant metabolism and/or livestock feeding studies.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

The enforcement method for the currently-established plant tolerances, including the currently-established soybean seed tolerance, is a high-performance liquid chromatography (HPLC) method with fluorescence detection (Method TMR0882B; D245477, S. Levy, 6-Jun-2001; D283827, W. Cutchin, 12-Jan-2005). An acceptable HPLC/mass spectrometry (MS)/MS confirmatory method is also available (Syngenta Method RAM 366/01; D283827, W. Cutchin, 12-Jan-2005). Since the introduction of the mesotrione-tolerant soybean does not result in a change in the tolerance expression, HED concludes that these methods are sufficient to enforce the tolerance recommend as part of the current review.

2.2.2 Recommended Tolerances

Table 2.2.2.1 is a summary of the proposed and HED-recommended tolerances for residues of mesotrione *per se*. A revised Section F is requested.

Table 2.2.2.1: Tolerance Summary.

Commodity	Proposed Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments
soybean, seed	0.02	0.03	Based on the available field trial data and the Organization for Economic Cooperation and Development (OECD) tolerance calculation procedure, a tolerance of 0.03 ppm is recommended.
soybean, flour	--	0.05	Soybean flour is not listed as a processed commodity in Table 1 and HED does not normally set tolerance in/on this commodity. However, since the available data demonstrated concentration and since the Canadian Pest Management Regulatory Agency (PMRA), which is also reviewing these data, will be setting a tolerance in/on soybean flour at 0.05 ppm, a tolerance is recommended herein.

2.2.3 Revisions to Petitioned-For Tolerances

Based on the available field trial data and the OECD tolerance calculation procedure, tolerances for residues of mesotrione *per se* in/on soybean seed and flour at 0.03 ppm and 0.05 ppm, respectively, are recommended.

2.2.4 International Harmonization

There are no Codex or Mexican maximum residue limits (MRLs) in/on the proposed commodities (see Attachment 1). The current action is being reviewed jointly with the Health Canada Pest Management Regulatory Agency (PMRA) with the PMRA and HED in agreement concerning the tolerance expression and values associated with the current action.

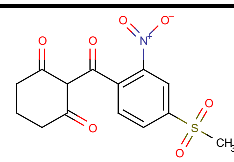
2.3 Label Recommendations

A revised Section B prohibiting the grazing/feeding of soybean forage/hay is requested.

3.0 Introduction

3.1 Chemical Identity

The chemical structure and nomenclature of mesotrione and its metabolite MNBA are presented in Tables 3.1.1.

TABLE 3.1.1. Test Compound Nomenclature.	
Chemical structure	
Common name	Mesotrione
Company experimental name	ZA1296
IUPAC name	2-(4-mesyl-2- nitrobenzoyl)cyclohexane-1,3-dione
CAS name	2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione
CAS registry number	104206-82-8
End-use product (EP)	4 lb/gal SC (Callisto® Herbicide; EPA Reg. No. 100-1131)

3.2 Physical/Chemical Properties

Table 3.2.1 is a summary of the physical/chemical properties for mesotrione. Mesotrione has a low vapor pressure, Log K_{ow}, and Henry's law constant (5.1 x 10^{-7} Pa m^3/mol).

TABLE 3.2.1. Physicochemical Properties of the Technical Grade Test Compound Mesotrione.		
Melting range	148.7-152.5°C	RD Memo; D263245, H. Podall, 24-Feb-2000
pH (25°C)	3.4 (1% dispersion in water)	
Density (20°C)	1.46 g/mL	
Water solubility (20°C)	160 ppm, unbuffered water 0.22 g/100 mL, pH 4.8 1.5 g/100 mL, pH 6.9 2.2 g/100 mL, pH 9	
Solvent solubility (20°C)	0.37 g/100 mL, methanol 1.7 g/100 mL, ethyl acetate 0.27 g/100 mL, toluene 10.4 g/100 mL, acetonitrile <0.03 g/100 mL, heptane 8.1 g/100 mL, acetone	
Vapor pressure (20°C)	4.3 x 10^{-8} torr	
Dissociation constant, pK_a (20°C)	3.12	
Octanol/water partition coefficient, Log(K_{OW}) (20°C)	log K_{OW} = 0.11 in unbuffered water log K_{OW} = 0.90 in pH 5 buffer log K_{OW} <-1 at pH 7 and 9 buffered water	
UV/visible absorption spectrum	Absorption maximum in methanol at 256 mu, with a molar extinction coefficient of 2.24 x 104 M cm.	

3.3 Pesticide Use Pattern/Directions

The petitioner provided a proposed label which included instructions for pre-/post-emergent application to mesotrione-tolerant soybean. Table 3.3.1 is a summary of the proposed formulated product and Table 3.3.2 is a summary of the proposed application scenario. The proposed label includes the following rotational crop restrictions: immediate - labeled crops; 120 days - small grains; 10 months - alfalfa, blueberry, canola, cotton, lingonberry, peanuts, potatoes, soybeans, sunflowers, and tobacco; 18 months - all other crops.

Provided the label is revised to prohibit the grazing/feeding of soybean forage/hay, HED concludes that the proposed application directions are adequate. A revised Section B is requested.

Table 3.3.1. Summary of Proposed Formulated Product.

Name (EPA Reg. No.)	Formulation	AI Concentration;	Weeds Controlled
Callisto® Herbicide (EPA Reg. No. 100-1131)	suspension-concentrate (SC)	4 lbs ai/gallon	annual broadleaf weeds

Table 3.3.2. Summary of Application Scenarios

Crop	Formulation	Method	Rate; lbs ai/acre	RTI (days)	PHI (days)	Comments[1]
mesotrione-tolerant soybean (SYNHT02R)	SC 4 lbs ai/gallon (see Table 3.3.1)	preplant incorporated, preplant, and preemergent	0.20	not specified	45	-Apply no more than 1 post-emergent app. and no more than 2 total apps. per year. -Do not apply more than 0.31 lb ai/acre/year. -Do not apply aerially or through irrigation equipment. -Apply in spray volumes of 10-60 gallons per acre (GPA) for pre-emergent application and 10-30 GPA for post-emergent application. -If weeds are emerged at the time of app., the addition of a non-ionic surfactant (NIS) or crop-oil concentrate (COC) is recommended as well as ammonium sulfate (AMS).
		Postemergent up to and including V2 crop stage	0.09-0.20			
		V3 crop stage up to and including R1 crop stage	0.09-0.11			

[1] NIS = nonionic surfactant; COC = crop oil concentrate; AMS = ammonium sulfate.

4.0 Metabolism/Degradate Residue Profile

Primary Crops: Field corn (preemergent and foliar application) and peanut (preemergent application) metabolism studies conducted with [cyclohexanedione-2-^{14}C]mesotrione and [^{14}C-phenyl]mesotrione and a cranberry (foliar application) metabolism study conducted with [^{14}C-phenyl]mesotrione were previously submitted and reviewed (D245477, S. Levy, 6-Jun-2001; D283827, W. Cutchin, 12-Jan-2005; D326898, S. Levy, 2-Mar-2007). The data reflecting application of [^{14}C-phenyl]mesotrione mesotrione to field corn, peanut, and cranberry indicate that the major metabolic pathway involves cleavage of the cyclohexanedione ring to yield MNBA, which is further reduced to its amino analog, AMBA. Mesotrione may also undergo hydroxylation to form 4-OH-mesotrione. The results of metabolism studies reflecting application of [cyclohexanedione-2-^{14}C]mesotrione mesotrione to field corn and peanut indicate that the cyclohexanedione ring may be degraded to CO_2 which is incorporated into natural products, and the cyclohexanedione ring may be oxidized to form 4-OH-mesotrione which is further metabolized to form multiple metabolites.

The field corn and peanut studies were deemed acceptable, and the results were shown to be similar. However, the cranberry data were deemed incomplete because metabolism data reflecting application with [cyclohexanedione-2-^{14}C]mesotrione were not submitted. Based on these data, HED concluded that the residue of concern in the currently-registered crops for tolerance expression and risk assessment purposes is mesotrione *per se*. It was noted that the requirements for plant metabolism data in three dissimilar crops had not been fulfilled, and that additional plant metabolism data may be required to support future uses on additional crops.

In support of the current petition, Syngenta submitted a mesotrione-tolerant soybean (SYHT04R soybean; see below) metabolism study conducted with [cyclohexanedione-2-^{14}C]mesotrione and [^{14}C-phenyl]mesotrione (48996202.der). The SYHT04R soybean received pre-emergent and foliar application using a scenario similar to the proposed application scenario. TRRs in the dried seed were low (0.039-0.104 ppm) with mesotrione, 4/5-hydroxy-mesotrione, MNBA, and/or AMBA identified at 3-10% TRR (total identified at 6-16% TRR). Excluding a polar unknown, unknowns were ≤10% TRR or ≤0.007 ppm. The polar unknown was found at 6-43% TRR with the study characterizing this unknown from the pre/post-cyclo seed sample (0.040 ppm; 43.0% TRR) as follows: (1) likely not conjugated and stable under mild and harsh acid hydrolysis; (2) multi-component with each ≤0.006 ppm; (3) molecular weight determination indicated multiple components each <1000Da; and (4) transitory since it declined/degraded rapidly based on TRR comparisons to the other seed samples with longer preharvest intervals (PHIs).

The study indicated that mesotrione is metabolized in SYHT04R soybean via hydroxylation of the cyclohexanedione ring followed by cleavage of the phenyl-cyclohexanedione ring bridge to form MNBA and AMBA; mesotrione and/or the identified metabolites may also be metabolized to a variety of minor metabolites and/or natural products. Based on these data, HED concludes that the nature of the residues in SYHT04R dried soybean seed following pre-emergent and foliar application is understood with mesotrione *per se* as the residue of concern for tolerance enforcement and risk assessment purposes. Since a grazing/feeding restriction for soybean forage/hay is required, defining the residues of concern in these commodities is unnecessary.

HED notes that the metabolism study was conducted with SYHT04R soybean while SYNHT02R soybean is the variety Syngenta will bring to market. Both of these varieties were genetically modified to express the avhppd-03 gene derived from oat (*Avena sativa* L.). SYNHT02R differs from SYHT04R in that it also contains the PAT gene from *Streptomyces viridochromogenes*; the PAT gene encodes the phosphinothricin acetyltransferase enzyme which acetylates glufosinate ammonium to the non-herbicidal N-acetyl glufosinate (see Attachment 4). The Food and Drug Administration review of glufosinate ammonium tolerant corn indicated that the phosphinothricin acetyltransferase enzyme derived from the *Streptomyces viridochromogenes* PAT gene is specific for glufosinate ammonium while not effecting L-glutamate or other amino acids (http://www.fda.gov/Food/FoodScienceResearch/Biotechnology/Submissions/ucm161145.htm). Based on the structurally similarity of glufosinate ammonium and glutamate and since the phosphinothricin acetyltransferase enzyme did not alter glutamate, HED concludes that it is unlikely that the phosphinothricin acetyltransferase enzyme will alter mesotrione or its metabolites. Therefore, the SYHT04R metabolism data are adequate to represent metabolism of mesotrione in SYNHT02R.

Rotational Crops: A confined rotational crop study conducted with cyclohexanedione-2-^{14}C]mesotrione and [^{14}C-phenyl]mesotrione has been previously submitted and reviewed (D274111, S. Levy, 26-Apr-2001; D245477, S. Levy, 6-Jun-2001). Wheat and soybeans were planted 30 days after soil treatment at ~0.275 lb ai/acre (1.4x/0.9x the proposed maximum single/seasonal rate). Endive, radish, and wheat were planted at 120 (both labels) and 300 (phenyl label only) days after soil treatment at 0.412 lb ai/acre (2.1x/1.3x the proposed maximum single/seasonal rate). The study indicated that leafy and root crops could not be planted at the 30 day interval because of phytotoxicity. Based on the identified residues, mesotrione is metabolized in rotational crops via a route similar to that demonstrated in primary crops. HED concluded that for tolerance expression and risk assessment purposes, the residue of concern in/on rotational crop commodities is mesotrione *per se*.

Livestock: Ruminant (dietary burden of ~10 ppm; 7 consecutive days) and poultry (dietary burden of ~10 ppm; 10 consecutive days) metabolism studies conducted with cyclohexanedione-2-^{14}C]mesotrione and [^{14}C-phenyl]mesotrione has been previously submitted and reviewed (D245477, S. Levy, 6-Jun-2001; D283827, W. Cutchin, 12-Jan-2005). Based on the results of the dairy cow metabolism studies, it was proposed that mesotrione is metabolized by the reduction of the nitro group to an amino group, leading to the formation of the metabolite AMBA. In addition, separation of the phenyl and cyclohexanedione rings may occur with the cyclohexanedione ring metabolized and incorporated into natural products such as lactose. In the poultry metabolism study, mesotrione was the primary residue found in eggs and edible tissues; however, incorporation into natural components such as palmitic, oleic, and stearic acid was also demonstrated. HED concluded that for tolerance expression and risk assessment purposes the residue of concern in/on livestock commodities is mesotrione *per se*.

5.0 Residue Profile

5.1 Residue Analytical Methods

5.1.1 Data-Collection Methods

The dried soybean seed raw agricultural commodity (RAC) and processed samples submitted in support of the current petition were analyzed for residues of mesotrione and its metabolite MNBA using Syngenta Method RAM 366/01. Briefly, samples were extracted with ACN:water (1:1, v:v) containing sodium chloride and centrifuged (addition of sodium chloride for the miso samples was deemed unnecessary). An aliquot of the extract was diluted with water and cleaned-up using an Oasis® HLB solid-phase extraction (SPE) cartridge eluted with methanol containing 2% formic acid (SPE clean-up was not performed for the 49191501.der samples). The eluant was concentrated to dryness, dissolved in water:methanol (9:1; v:v), and analyzed via HPLC/MS/MS. Based on the lower limit of method validation (LLMV), the limit of quantitation (LOQ) was 0.01 ppm for both analytes/matrices (limit of detection was not reported). It is noted that the study did not report MNBA residues in parent equivalents. However, based on the molecular weights for each compound, the LOQ for MNBA in parent equivalents is 0.014 ppm, which rounds to 0.01 ppm. It is noted that the Method RAM 366/01 employs the same extraction solvents as the current enforcement method.

5.1.2 Multiresidue Methods

The Food and Drug Administration (FDA) multiresidue method (MRM) data were previously submitted and forwarded to FDA (D260571, S. Levy, 16-Nov-1999). The FDA PESTDATA database dated 06/05 (PAM Volume I, Appendix I) indicates that mesotrione is not recovered using MRM Sections 302 (Luke Method; Protocol D). No recovery data pertaining to MRM Section 303 (Mills, Onley, and Gaither Method; Protocol E, nonfatty food) or 304 (Mills Method; Protocol F, fatty food) were included. The MRMs are not adequate for enforcement.

5.1.3 Tolerance-Enforcement Method

The enforcement method for the currently-established plant tolerances, including the currently-established soybean seed tolerance, is a HPLC method with fluorescence detection (Method TMR0882B; D245477, S. Levy, 6-Jun-2001; D283827, W. Cutchin, 12-Jan-2005). The confirmatory method for tolerance enforcement is the data-collection method summarized above (Syngenta Method RAM 366/01; D283827, W. Cutchin, 12-Jan-2005). Since the introduction of the mesotrione-tolerant soybean does not result in a change in the tolerance expression, HED concludes that these methods are sufficient to enforce the tolerance recommend as part of the current review.

Tolerance-Enforcement Method TMR0882B: In brief, residues of mesotrione are extracted with acetonitrile (ACN):water (1:1, v:v). An aliquot of the extract is concentrated to the aqueous phase, brought to volume with formic acid in water, and purified by reverse-phase HPLC on a Phenomenex Prodigy C18 column. The mesotrione fraction is collected and mesotrione is oxidized to MNBA using a 30% hydrogen peroxide solution heated at 85° C for 20 minutes followed by reduction to AMBA by heating at 65° C for 20 minutes with a solution of stannous chloride reagent and 2N HCl. After final cleanup on a Bond Elut LRC C18 SPE column, residues are quantified by using a reverse-phase HPLC equipped with a Phenomenex Prodigy C18 column and a fluorescence detector.

5.1.4 Submittal of Analytical Reference Standards

Analytical standards for mesotrione (expiration date 28-Feb-2016), MNBA (expiration date 31-Oct-2015), and AMBA (expiration date 30-Apr-2016) are available at the EPA National Pesticide Standards Repository (e-mail from Theresa Cole; 20-Oct-2014).

5.2 Storage Stability

Soybean seed samples were stored frozen for 14.1 months prior to analysis and soybean meal, hulls, oil, AGF, flour, milk, tofu, soy sauce, and miso were stored frozen for up to 123 days prior to analysis. Data has been previously submitted demonstrating the stability of fortified residues of mesotrione and MNBA in/on field corn forage, stover, and grain (42 months); radish root (44 months); and soybean seed (40 months; D245477, S. Levy, 6-Jun-2001). No data are available reflecting the storage stability of residues of mesotrione or MNBA in/on any processed commodity. Based on the extended interval and diversity of commodities from the available storage stability data (high oil/protein content, high starch content, and high water content) and the relatively short storage interval for the processed samples (≤123 days), HED concludes that the available storage stability data are adequate.

5.3 Residue Data

5.3.1 Crop Field Trials

Mesotrione is currently registered for preemergent application to mesotrione-tolerant soybean with an established tolerance for residues of mesotrione *per se* in/on soybean seed of 0.01 ppm (grazing/feeding soybean forage/hay is prohibited; D358159, S. Levy, 5-Aug-2009). Syngenta is proposing pre-/post-emergent application to mesotrione-tolerant soybean and the establishment of a soybean seed tolerance for residues of mesotrione *per se* of 0.02 ppm (grazing/feeding restrictions are required). In conjunction with the current registration, Syngenta will market the SYNHT02R soybean variety and indicated that this variety has been genetically modified to express the avhppd-03 gene derived from oat (*Avena sativa* L.) and the PAT gene from *Streptomyces viridochromogenes* (e-mail from Dr. Jerry Wells of Syngenta to Michael Walsh of RD). The avhppd-03 gene confers tolerance to mesotrione as it encodes a HPPD enzyme with a lower binding affinity to mesotrione than the native HPPD enzyme. The PAT gene encodes the enzyme phosphinothricin acetyltransferase which acetylates the active ingredient glufosinate (glutamine synthetase inhibitor) to the non-herbicidal N-acetyl glufosinate.

In support of the current proposal, the petitioner submitted magnitude of the residue studies conducted with the mesotrione-tolerant soybean varieties SYHT04R (48996201.der; n=20) and SYHT0H2 (49191501.der; n=6). SYHT04R differs from SYHT0H2 in that it does not include the PAT gene. The application scenarios employed in these studies are an adequate representation of the proposed application scenario and the samples were analyzed for residues of mesotrione and MNBA using an adequately validated method (storage intervals have also been validated). Residues of mesotrione were ≤0.025 ppm and residues of MNBA were <0.01 ppm (<LOQ; soybean variety did not influence the magnitude of the residue). A summary of these studies is presented below.

<u>*48996201.der:*</u> Twenty field trials were conducted in the United States during the 2009 growing season, using the mesotrione-tolerant soybean variety SYHT04R, in the North American Free Trade Agreement (NAFTA) Growing Zones 2 (2 trials; NC and SC); 4 (3 trials; AR, LA, and MO); 5 (14 trials; IA (n=5), MO (n=3), KS, NE (n=3), OH (n=2)); and 5a (1 trial; MI). Each field site consisted of one untreated plot and 2 or 3 treated plots with the treated plots receiving application of Callisto® 4SC (4 lb ai/gallon; EPA Reg. No. 100-1131) as described in the Table 5.3.1.1. Spray volumes were 6-30 GPA. All of the spray solutions included AMS and either a COC or a NIS excluding the first application at Proctor, AR (treatment method #2) and Richland,

IA (treatment method #2) trials were no adjuvants were included. Application method #4 was included at each of the trials with application method #2 included at 10 of the trials and application method #3 included at 11 of the trials. Samples of dried soybean seed were harvested at the PHIs indicated in the Table 5.3.1.1 (forage and hay samples were not collected). At two of the application method #4 plots, residue decline samples were also collected 7 days prior to normal harvest, at normal harvest, and at 7 and 14 days after normal harvest. It is noted that only a single sampling interval was required for the Elko, SC (application methods #3 and #4) and Washington, LA (application methods #3 and #4) trials as the early sample represented the mature soybean seed.

Table 5.3.1.1. Summary of Application Scenarios and PHIs.

Application Method	Method and timing	Rate lb ai/acre	n	PHI (days)
1	control		20	Dried soybean seed samples were harvested ~45 days after the R1 stage and at maturity.
2	preplant incorporated	0.201	10	Dried soybean seed samples were harvested 45-50 days after the last application (DALA) and at maturity 55-102 DALA.
	foliar broadcast spray at R1 crop stage	0.111		
3	broadcast soil application at planting	0.201	11	Dried soybean samples were harvested 43-58 DALA and at maturity 58-123 DALA.
	foliar broadcast spray at R1 crop stage	0.111		
4	foliar broadcast spray at V2 crop stage	0.201	19[1]	Dried soybean seed samples were harvested 59-83 DALA (~45 days after the R1 stage) and at maturity 72-145 DALA.

[1] The Richwood, OH treatment plot #4 samples are not included as the application rate was 0.067 lb ai/acre (residues were <LOQ).

Residues of mesotrione and its metabolite MNBA were determined in/on the dried soybean seed samples using an adequately validated method (Syngenta Method RAM 366/01); storage intervals have also been validated. Residues of MNBA were <0.01 ppm in/on all the dried soybean seed samples; residues of mesotrione were as follows: (1) application method #2 - ≤0.01 ppm (~45 day PHI) and ≤0.02 ppm (mature); (2) application method #3 - ≤0.02 ppm (~45 day PHI and mature); and (3) application method #4 - <0.01 ppm in/on all samples. Evaluation of residue decline is not possible as residues were <LOQ in/on all of the residue decline samples. Table 5.3.1.2 is a summary of the residue data.

49191501.der: Six field trials were conducted in the United States during the 2012 growing season, using the SYHT0H2 soybean variety, in the NAFTA Growing Zone 5 (IA (n=4), MN (n=1), and NE (n=1)). Each field site consisted of one untreated plot and one treated plot with the treated plots receiving application of Callisto 4SC (4 lb ai/gallon; EPA Reg. No. 100-1131) as either a broadcast application at planting (n=3) or a preplant soil incorporated application (n=3) at 0.200-0.211 lb ai/acre; this was followed at all sites by a foliar broadcast spray application at the R1 crop stage (0.108-0.114 lb ai/acre). Spray volumes were 18-30 GPA. All of the spray solutions included AMS and either a COC or a NIS. Dried soybean seed was harvested at normal commercial maturity 77-106 DALA (forage and hay samples were not collected).

Residues of mesotrione and its metabolite MNBA were determined in/on the dried soybean seed samples using an adequately validated method (Syngenta Method RAM 366/01); storage intervals have also been validated. Residues of MNBA were <0.01 ppm in/on all the dried soybean seed samples. Residues of mesotrione in/on the dried soybean seed samples were <0.01 ppm in/on all samples except for one which had residues of 0.025 ppm. Table 5.3.1.2 is a summary of the residue data.

TABLE C.4. Summary of Residue Data.

Commodity	App. Method	Total Rate; lb ai/acre (g ai/hectare)	PHI (days)	Residues of Mesotrione (ppm)[1]							
				n	Min.	Max.	LAFT	HAFT	Median	Mean	Std. Dev.
dried soybean seed SYHT04R; 48996201.der[2]	2	0.311-0.317 (349-355)	45-50	10	<0.01	0.01	<0.01	<0.01	0.01	0.01	--
			55-102	10	<0.01	0.02	<0.01	0.02	0.01	0.01	0.003
	3	0.306-0.321 (343-360)	43-49	11	<0.01	0.02	<0.01	0.02	0.01	0.01	0.002
			58-123	11	<0.01	0.02	<0.01	0.02	0.01	0.01	0.003
	4[3]	0.198-0.208 (222-233)	59-83	19	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	--
			75-145	17	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	--
dried soybean seed SYHT0H2; 49191501.der	2	0.312-0.323 (350-362)	90-97[4]	6	<0.01	0.025	<0.01	0.025	0.010	0.015	0.008
	3	0.314-0.323 (352-362)	77-106[4]	6	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	--

[1] Excluding min and max, summary statistics are based on per-trial average residues, Residues <LOQ were assumed to be equal to the LOQ for calculation of the median, mean, and standard deviation (if all residues were <LOQ then the summary statistics were reported as such). LAFT = lowest-average field trial and HAFT = highest-average field trial. The study did not report residues of MNBA in parent equivalents (all MNBA residues were <0.01 ppm). However, based on the molecular weights for each compound, a 0.01-ppm MNBA residue converts to an MNBA residue in parent equivalents of 0.014 ppm which rounds to 0.01 ppm.

[2] Following treatment under application method #2, dried soybean seed samples were harvested 45-50 DALA (last application at R1 stage) and at maturity 55-102 DALA. Following treatment under application method #3, dried soybean seed samples were harvested 43-58 DALA (last application at R1 stage) and at maturity 58-123 DALA. Following treatment under application #4, dried soybean seed samples were harvested 59-83 DALA (~45 days after R1 stage) and at maturity 72-145 DALA. Only a single sampling interval was required for the Elko, SC (application methods #3 and #4) and Washington, LA (application methods #3 and #4) trials as the early sample represented the mature soybean seed.

[3] The Richwood, OH treatment plot #4 samples are not included as the application rate was 0.067 lb ai/acre (75 g ai/hectare; residues were <LOQ).

[4] Dried soybean seed samples harvested at maturity.

5.3.2 Field Rotational Crops

An acceptable limited field rotational crop study was previously submitted and reviewed (D245477, S. Levy, 6-Jun-2001). Following a single preplant incorporated application made to the primary crop (field corn) at 0.30 lb ai/acre (1.5x/1.0x the proposed single/seasonal rate), residues of mesotrione and its metabolite MNBA were less than the method LOQ (<0.01 ppm) in/on all rotational crop matrices planted 29-30 days after application (radish roots and tops; soybean forage, hay, and seed; millet forage, hay, straw, and grain; and sorghum forage). In addition, following preplant incorporated (0.30 lb ai/acre) and postemergence (0.20 lb ai/acre) application to the primary crop (field corn; 1.5-1.0x/1.6x the proposed single/seasonal rate), residues of mesotrione and its metabolite MNBA were each less than the method LOQ (<0.01 ppm) in/on all rotational crop matrices planted 74-100 days after application (radish roots and tops; endive leaves; and wheat forage, hay, straw, and grain). Based on these data, HED concludes that the proposed rotational crop restrictions are acceptable and tolerances in/on rotational crops are not required.

5.3.3 Processed Food/Feed

The petitioner submitted an adequate soybean processing study (48996201.der2; see below for summary). Dried soybean seed samples (SYHT04R variety) were collected from two trials treated with Callisto 4SC (4 lb ai/gallon; EPA Reg. No. 100-1131) at 5x the proposed single/seasonal rate (76-108 DALA). The seed samples were processed into AGF, hulls, meal, crude oil, refined oil, flour, milk, tofu, soy sauce, and miso using simulated commercial practices. Residues of mesotrione and MNBA were determined using an adequately validated method (Syngenta Method RAM 366/01; storage intervals also been validated).

Residues of MNBA were <LOQ in/on all commodities. For one of the trials, residues of mesotrione were <LOQ in/on all commodities except soybean refined oil (<0.01-0.01 ppm) and flour (0.02 ppm). Based on these data, residues of mesotrione concentrated in/on soybean refined oil and flour at >1.0x and >2.0x respectively. For the other trial, residues of mesotrione were <LOQ in/on all commodities except the soybean seed RAC (0.04 ppm), soybean hulls (0.01-0.02 ppm), meal (0.01 ppm), refined oil (<0.01-0.01 ppm), AGF (0.02 ppm), and flour (0.07 ppm). Based on these data, residues of mesotrione concentrated in/on soybean flour (1.75x) and reduced in hulls (0.50x); AGF (0.50x); meal (0.25x); refined oil (0.25x); and crude oil, milk, tofu, soy sauce, and miso (<0.25x). The theoretical concentration factors for soybean, based on separation into components, are 11.3x for soybean hulls, 2.2x for soybean meal, and 12.0x for soybean oil (OPPTS 860.1520, Table 3).

HED will rely on the data from the trial which yielded quantify residues in/on the soybean RAC. Based on these data, HED concludes that a tolerance in/on soybean flour of 0.05 ppm is appropriate (0.025 x 1.75 = 0.044 ppm); tolerances in/on the remaining soybean processed commodities are unnecessary. It is noted that soybean flour is not listed as a processed commodity in Table 1. However, since the available data demonstrated concentration and since PMRA, which is also reviewing these data, will be setting at tolerance in/on soybean flour at 0.05 ppm, a tolerance is recommended herein.

48996201.der2: Two field trials were conducted in the United States during the 2009 growing season, using the mesotrione-tolerant soybean variety SYHT04R (Richland, IA and Bagly, IA). The treated plots received application of Callisto 4SC (4 lb ai/gallon; EPA Reg. No. 100-1131) as either a broadcast application at planting (Bagley, IA) or a preplant soil incorporated application (Richland, IA) at 1.008-1.023 lb ai/acre; this was followed at both sites by a foliar broadcast spray application at the R1 crop stage (0.556-0.572 lb ai/acre; 5.0x the proposed single/seasonal rate). Mature soybean seed was harvested 76-108 DALA and processed into AGF, hulls, meal, crude oil, refined oil, flour, milk, tofu, soy sauce, and miso using simulated commercial practices.

Residues of mesotrione and its metabolite MNBA (2-nitro-4-(methylsulfonyl)benzoic acid) were determined using an adequately validate method (storage intervals were also validated). For the Richland, IA trial, residues of MNBA were <LOQ in/on all commodities and residues of mesotrione were <LOQ in/on all commodities except soybean refined oil (<0.01-0.01 ppm) and flour (0.02 ppm). Based on these data, residues of mesotrione concentrated in/on soybean refined oil and flour at >1.0x and >2.0x respectively. For the Bagly, IA trial, residues of MNBA were <LOQ in/on all commodities and residues of mesotrione were <LOQ in/on all commodities except the soybean seed RAC (0.04 ppm), soybean hulls (0.01-0.02 ppm), meal (0.01 ppm), refined oil (<0.01-0.01 ppm), AGF (0.02 ppm), and flour (0.07 ppm). Based on these data, residues of mesotrione concentrated in/on soybean flour (1.75x) and reduced in hulls (0.50x); AGF (0.50x); meal (0.25x); refined oil (0.25x); and crude oil, milk, tofu, soy sauce, and miso (<0.25x). The theoretical concentration factors for soybean, based on separation into components, are 11.3x for soybean hulls, 2.2x for soybean meal, and 12.0x for soybean oil (OPPTS 860.1520, Table 3).

5.3.4 Meat, Milk, Poultry, and Eggs

HED previously calculated ruminant, poultry, and hog dietary burdens of 0.461-0.526 ppm, 0.010 ppm, and 0.009 ppm, respectively, and concluded that that at these dietary burdens and based on the metabolism studies, there was no reasonable expectation of quantifiable mesotrione residues of concern in meat, milk, poultry, or eggs (Category 180.6(a)(3); D326898, S. Levy, 2-Mar-2007; D383827, W. Cutchin, 12-Jan-2005). Based on the revised Table 1 feedstuffs and the recommended soybean seed tolerance of 0.03 ppm (seed tolerance covers the processed commodity tolerances), the current petition will not have a significant effect on the ruminant dietary burden. The current petition will result in an increase in the poultry (0.015 ppm) and hog (0.013 ppm) dietary burdens. As explained below, this increase does not alter the previous conclusions concerning no reasonable expectation of residues. However, future proposed uses may require ruminant and/or poultry feeding studies.

Poultry: The poultry metabolism study resulted in TRRs of ≤1.245 ppm in egg, muscle, fat, and liver following dosing for ten consecutive days at 10 ppm (667x). Dividing the 1.245 ppm residue by 667x, yields a residue estimate of 0.002 ppm. Based on this estimate and the conservative nature of the dietary burden calculations, HED concludes that residues in poultry will be negligible.

Hog: The ruminant metabolism study resulted in TRRs of ≤0.110 ppm in milk, muscle, fat, kidney, and liver following dosing for ten consecutive days at 10 ppm (769x). Dividing the 0.110 ppm residue by 769x, yields a residue estimate of 0.0001 ppm. Based on this estimate and the conservative nature of the dietary burden calculations, HED concludes that resides in hog will be negligible.

5.4 Food Residue Profile

Mesotrione is currently registered for application to asparagus, berry group 13, field corn, seed corn, yellow popcorn, sweet corn, cranberry, flax, grasses grown for seed, lingonberry, pearl millet, oat, okra, rhubarb, sorghum (sweet and grain), soybean, and sugarcane with tolerances for residues of mesotrione *per se* in/on the food commodities associated with these crops of 0.01-0.02 ppm (LOQ = 0.01 ppm). The residues data submitted in conjunction with the current petition were similar with residues of mesotrione *per se* in/on dried soybean seed of ≤0.025 ppm. The soybean processing study resulted in a reduction in mesotrione *per se* residues for all processed commodities excluding soybean flour where residues were shown to concentrate 1.75x. Based on the current livestock dietary burdens and the results of the ruminant and poultry metabolism studies, residues in livestock will be insignificant. Also, based on the rotational crop PBIs and the result of the confined and field rotational crop studies, residues in rotational crops will be insignificant.

6.0 Tolerance Derivation

In support of the current proposal, the petitioner submitted magnitude of the residue studies conducted with the mesotrione-tolerant soybean varieties SYHT04R (48996201.der; n=20) and SYHT0H2 (49191501.der; n=6). The geographical representation for the trials conducted with the SYHT04R variety fulfill the requirements suggested in OPPTS 860.1500 for soybean. The SYHT0H2 residue data were submitted to demonstrate that the magnitude of the residues in this variety, which will be brought to market, is similar to SYHT04R (similarity was demonstrated). The studies resulted in residues of mesotrione in/on dried soybean seed of ≤0.01 ppm in all cases except for one sample collected from each study where residues were 0.02 ppm (SYHT04R) and 0.025 ppm (SYHT0H2). To determine the appropriate tolerance, the OECD tolerance-calculation procedure was employed and residue values of 0.01 ppm were assumed for all samples except for two where residues of 0.02 ppm and 0.025 ppm were assumed. Based on these assumptions and using the OECD tolerance-calculation procedure, a tolerance of 0.03 ppm for residues of mesotrione *per se* in/on soybean seed is recommended (see Attachment 2). Based on the processing data which demonstrated that residues of mesotrione *per se* concentrate in/on soybean flour (1.75x) and the HAFT for soybean seed (0.025 ppm), HED is recommending for a tolerance in/on soybean flour of 0.05 ppm (1.75 x 0.025 = 0.044 ppm). Table 6.0.1 is a summary of the petitioner proposed and HED recommended tolerance for residues of mesotrione *per se*.

Table 6.0.1: Tolerance Summary.

Commodity	Proposed Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments
soybean, seed	0.02	0.03	Based on the available field trial data and the OECD tolerance-calculation procedure, a tolerance of 0.03 ppm is recommended.
soybean, flour	--	0.05	Soybean flour is not listed as a processed commodity in Table 1 and HED does not normally set tolerance in/on this commodity. However, since the available data demonstrated concentration and since PMRA, which is also reviewing these data, will be setting a tolerance in/on soybean flour at 0.05 ppm, a tolerance is recommended herein.

Attachment 1: International Residue Limits.
Attachment 2: OECD Tolerance Calculations.
Attachment 3: Chemical Names and Structures.
Attachment 4: PAT Mediated Acetylation of Glufosinate Ammonium.

RDI: RAB1 Chemists (2-Oct-2013)

Attachment 1: International Residue Limits.

Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition				
US		Canada	Mexico[2]	Codex
mesotrione (2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione)		2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione	--	None
Tolerance/Maximum Residue Limit (ppm)				
Commodity[1]	US	Canada	Mexico[2]	Codex
soybean, dried seed	0.03	0.01 dry soybeans[3]	--	--
soybean, flour	0.05	--	--	--
Completed: M. Negussie: 09/19/2013				

[1] Includes only commodities of interest for this action. Tolerance values are HED recommendations and not those proposed by the applicant.
[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.
[3] This is the currently-established Canadian tolerance. The current action is being reviewed jointly with PMRA with the PMRA and HED are in agreement concerning the tolerance expression and values associated with the current action.

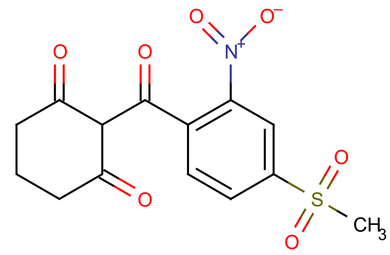
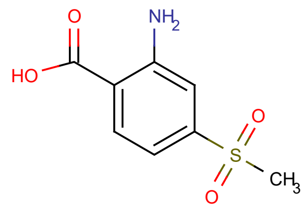
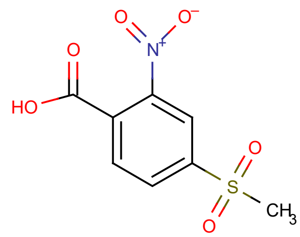
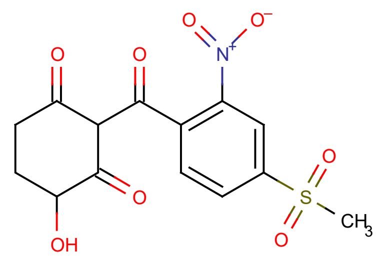
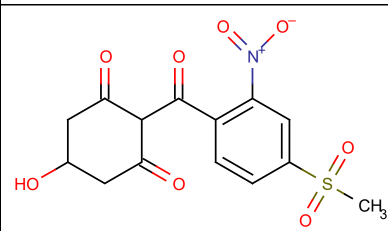
Attachment 2: OECD Tolerance Calculations.

Compound	mesotrione
Crop	soybean
Region / Country	U.S.A.
GAP	
Total number of data (n)	20
Percentage of censored data	85%
Number of non-censored data	3
Lowest residue	0.010
Highest residue	0.025
Median residue	0.010
Mean	0.011
Standard deviation (SD)	0.004
Correction factor for censoring (CF)	0.433
Proposed MRL estimate	
- Highest residue	0.025
- Mean + 4 SD	0.027
- CF x 3 Mean	0.015
Unrounded MRL	0.027
Rounded MRL	0.03

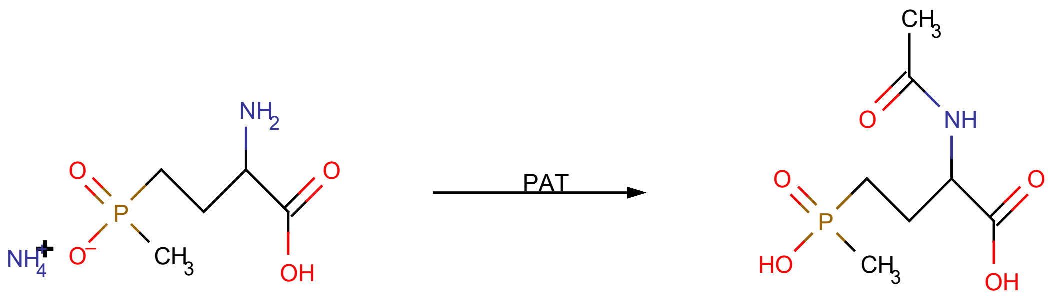
High uncertainty of MRL estimate due to high level of censoring.

Residues (mg/kg)	
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	
0.020	
0.025	

Attachment 3: Chemical Names and Structures.

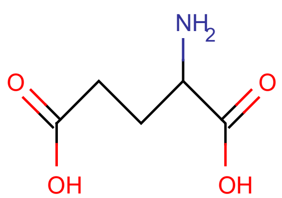
Common name/code	Chemical name	Chemical structure
mesotrione/ZA1296	CAS: 2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione IUPAC: 2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione	
AMBA/NOA 422848	2-amino-4-(methylsulfonyl)benzoic acid	
MNBA/NOA 437130	2-nitro-4-(methylsulfonyl)benzoic acid	
4-hydroxymesotrione/R282813	--	
5-hydroxymesotrione	--	

Attachment 4: PAT-Mediated Acetylation of Glufosinate Ammonium.



glufosinate ammonium N-acetyl-glufosinate

The Food and Drug Administration review of glufosinate ammonium tolerant corn indicated that the phosphinothricin acetyltransferase enzyme derived from the *Streptomyces viridochromogenes* PAT gene is specific for glufosinate ammonium while not effecting L-glutamate or other amino acids (http://www.fda.gov/Food/FoodScienceResearch/Biotechnology/Submissions/ucm161145.htm).



glutamate